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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/813,829	03/06/1997	BRIGID L. M. HOGAN	16016.0005	3939

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	28

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
08/813,829	Hogan, B.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 9, 2003*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *4* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *4* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on April 9, 2003, paper number 27, has been entered.

DETAILED ACTION

This application is a continuation of 08/217,921, filed March 25, 1994, now US Patent 5,690,926, and is a continuation-in-part of and a divisional of 07/958,562, filed October 8, 1992, now US Patent 5,453,357.

Claim 4 is pending and currently under examination.

Applicant has not filed claim amendments nor provided additional arguments with the instant request for the continued prosecution application 08/813,829. Therefore, all claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d). Thus, the grounds of rejection set forth in the Final Office Action, paper number 24, are maintained. The basis of the final rejections are reiterated below for Applicants' convenience.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 4 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a human pluripotential cell, does not reasonably provide enablement for human pluripotential stem cell wherein the characteristics of the cell includes having a normal karyotype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant points out that the methods and results disclosed in the instant specification demonstrate that some of the resulting stem cells in the derived mouse ES cell lines do have a normal karyotype. Further, based on the evidence that some mouse ES cells do have a normal karyotype, one of skill in the art could use the same methods to derive human ES cells having a normal karyotype. Applicants argue that case law does not require operability of every cell made, only that the artisan could practice the claimed method without undue experimentation. In addition, Applicants have provided post filing art to demonstrate that human ES cells are euploid. See Applicants amendment, pages 3-4. Applicants arguments have been fully considered but not found persuasive.

Lacking evidence to the contrary, Examiner would concede that some of the mouse ES cells in the derived ES cell lines may have a normal karyotype. However, as noted previously, the art of isolating pluripotential ES-like cells is not well established and highly unpredictable (paper number 8; pages 2-4). Examiner agrees that every embodiment need not be operable nor that a disclosure provide working examples of the claimed invention. The instant disclosure does not reduce to practice human ES cells, nor does the art at the time of filing teach these cells. In attempt to evaluate whether the instantly claimed human ES cells can be derived by the methods instantly disclosed, an evaluation of the state of the art was made. As noted previously, Piedrahita *et al.* teach that porcine and ovine embryos respond differently to the same treatments and that conditions that allowed the production of porcine ES-like cells did not allow development of ovine ES-like cells (page 886; Table 1 and page 888). Further, Cruz *et al.* teach that the embryonic development of different mammals varies, and thus, depending on the time and location of the isolation of the cell from the embryo, the nature of a cell isolated from said embryo can also vary. Thus, it was maintained that methods to isolate a pluripotential cell from one mammal cannot be extrapolated for use in another mammal to obtain a similar cell from a second species of mammal. Even the instant specification indicates that the characteristics of a cell derived with the claimed methods can not be predicted, and may actually be different from other ES cells or pluripotential cells which have already been derived. In light that some of the mouse ES cells may have a normal karyotype, Examiner would concede that it would not be an undue burden to practice the disclosed methods to generate a mouse ES cell, however the art

would support that these methods would not necessarily extrapolate to successful methods in isolating human ES cells. Even though pluripotential murine cells with a normal karyotype and could be isolated using the methods taught in the instant specification, in light of the unpredictability of the art in generating pluripotential cells, there is no clear nexus that methods used successfully to generate a mouse cell with a normal karyotype can be used to generate pluripotential cells with a normal karyotype from other mammals.

Upon review of the post filing art of Donovan *et al.*, it is noted that the human ES cells described are pluripotent. However, the evidence that a human ES cell is euploid is absent. The specification as summarized in Table 1, merely recites characteristics one may expect in EC, ES and EG cell lines for comparison. Further, even if were one to concede that the human ES cells discussed in Donovan *et al.* were euploid, there is no clear teaching on what methods were used to derive such human cells. Thus, the references fails to provide a nexus between the human ES cells discussed therein and those instantly claimed. In view of the art, the ability to isolate a human ES cell with the available methodology used in mouse ES cells would not have been considered predictable. Further, since the art supports that methods for one species can not simply and successfully be extrapolated to that of another, the type of experimentation required would to produce an human ES cell be empirical. In view of all the potential and possible variations for times of isolation from the embryo, culturing conditions for maintaining a pluripotential cell, and the failure of the art and the instant disclosure to demonstrate any condition which results in a human ES cell with a normal karyotype, it is maintained that the

skilled artisan would be subject to undue empirical experimentation without any expectation of success.

Thus, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art at the time the claimed invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed. Therefore, for the reasons above and of record, the rejection is maintained.

Conclusion

No claim is allowed.

Claim 4 is free of the art of record, however it is subject to other rejections.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630